

Application No. 10/777,043

Docket No.: 21095-00008-US1

**AMENDMENTS TO THE SPECIFICATION****RECEIVED  
CENTRAL FAX CENTER**Please replace paragraph beginning on page 1, line 36, with the following rewritten paragraph: **JUL 24 2006**

The invention relates to the chronic elevation of endogenous adenosine levels by the use of stable adenosine 5'-triphosphate (ATP) compositions, which are taken orally over a period of time. The elevated levels of adenosine, produced by the *in vivo* degradation of ATP, act in decreasing the sensitivity (desensitization) of adenosine receptors. The decrease in sensitivity can materialize through a decrease in numbers of receptors (density) or through a reduction in the receptor's coupling activity (intracellular signal transduction). The reduced sensitivity of certain adenosine receptors towards their natural agonist - adenosine, can be useful by itself or in combination with adenosine antagonists, which are much more active towards desensitized adenosine receptors. Examples for utilization of these methods are in the treatment of disorders or diseases, which are controlled by biochemical mechanisms regulated by adenosine receptors. One such case is in the treatment of obesity, which can be treated by the metabolic stimulation of weight loss. Lipolysis, the degradation of fat (triglycerides) in adipose tissue to free fatty acids and glycerol, is known to be inhibited by the interaction of adenosine with A<sub>1</sub> adenosine receptors of the adipocyte (fat cell). The interaction of adenosine with adipose tissue A<sub>1</sub> adenosine receptors was shown to stimulate lipogenesis- the buildup of triglycerides (fat) in fat cells. Methods for desensitization of A<sub>1</sub> adenosine receptors in a human *in vivo*, thus significantly diminishing the activity of endogenous adenosine, are disclosed and taught and are utilized for the effective reduction of weight in humans. Effective ~~weigh~~ weight loss in humans can be achieved either by the desensitization of the adipose tissue adenosine A<sub>1</sub> receptors by themselves, or by desensitization in combination with adenosine antagonists such as caffeine or theophylline, which are much more effective in blocking the action of adenosine once its receptors became desensitized. The use of chronic administration of adenosine for the purpose of desensitization of adipose tissue A<sub>1</sub> adenosine receptors in the induction of weight loss in humans, demonstrates the utility of the present invention. Obesity is the costliest disease in industrialized countries. It is associated with a variety of chronic life-threatening diseases such as type II diabetes, hypertension, stroke, and heart disease. The definition of obesity is an excessive accumulation of fat in the body. Obesity in terms of a disease is defined if body weight is 20% or more above the desirable weight (Council on Scientific Affairs, J. Amer. Med. Assoc. 1988). Overweight is defined if body weight exceeds the desirable weight by less than 20%. Desirable weight in humans has been well-defined (council on scientific affairs, JAMA 1988). Weight loss in overweight or obese humans can be achieved by diet, physical activity and behavior modification or by treatment with drugs. There are three main ways for the pharmaceutical

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treatment of overweight or obesity: 1. Inhibition of absorption of nutrients in the intestine; 2. Modulation of the activities of the metabolic and central nervous system (hypothalamic) satiety and food consumption (hunger) signals; and 3. Induction of energy dissipation in tissues, especially adipose tissue (thermogenesis). The methods disclosed here of the chronic administration of adenosine by the oral delivery of the pro-drug ATP, deal with the induction of energy dissipation, in the form of degradation of fats in adipose tissue.